

THE ASSOCIATION OF PREPREGNANCY BODY MASS INDEX, GESTATIONAL
WEIGHT GAIN, AND CHILD BIRTH WEIGHT WITH MARKERS OF
METABOLIC DYSFUNCTION IN OBESE CHILDREN
AND ADOLESCENTS

by

Kelsey Ann Pearson

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STATEMENT OF THESIS APPROVAL

The thesis of Kelsey Ann Pearson
has been approved by the following supervisory committee members:

Kristine Jordan, Chair 3/8/17
Date Approved

Nicole Mihalopoulos, Member 3/8/17
Date Approved

Julie Metos, Member 3/8/17
Date Approved

and by Scott Summers, Chair of

the Department of Nutrition and Integrated Physiology

and by David B. Kieda, Dean of The Graduate School.

ABSTRACT

Previous studies have reported that maternal prepregnancy body mass index (BMI), gestational weight gain (GWG), and child birth weight are positively associated with cardio-metabolic risk factors. Physical activity and dietary habits may play a role in reducing these risk factors. The purpose of this study was to investigate the association of prepregnancy BMI, GWG, child birth weight, physical activity, and dietary habits with metabolic dysfunction. Participants (n=124) included obese children and adolescents aged 8-17. In a fasted state, serum glucose, serum insulin, and a complete lipid profile were obtained. Anthropometrics, including body weight, height, and waist circumference, blood pressure, and self-reported survey responses were assessed as well. The chi-squared and Mantel-Haenzel test statistic were used to examine the differences in proportions for the outcome of metabolic dysfunction. In this sample, 76.9% of children and adolescents had metabolic dysfunction. Child birth weight was positively correlated ($p=0.033$) with a diagnosis of metabolic dysfunction. Sedentary behavior was positively related ($p=0.015$) with metabolic dysfunction; however, physical activity levels were not. Contrary to previous studies, prepregnancy BMI and GWG were not correlated with a diagnosis of metabolic dysfunction. More research is needed to determine the relationship between prepregnancy BMI, GWG, and child birth weight. These findings support the need for lifestyle interventions in obese children and adolescents, particularly in reducing sedentary behaviors in this population.

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INTRODUCTION

Background/Literature Review

Obesity is one of the most challenging health problems facing our society today. According to the National Health and Nutrition Examination Survey (NHANES) 2009–2010, more than 2 out of 3 adults in the United States are overweight (Body Mass Index (BMI) ≥ 25 kg/m²) or obese (BMI ≥ 30 kg/m²) [1, 2]. As with all groups, pregnant women and women of child bearing age are becoming more overweight, with a 58% increase in rate from 1976-2004 [3]. Women of low socioeconomic status and minority groups are disproportionately affected by increasing obesity rates [5].

According to the Pregnancy Risk Assessment Monitoring System (PRAMS), 1 in 5 American women are obese at the time of conception [3]. During pregnancy, it has been estimated that 40% of women gain excessive weight [4]. Furthermore, the Committee to Reexamine the Institute of Medicine (IOM) Pregnancy Weight Guidelines reported excess gestational weight gain (GWG) in 38.4% of normal weight, 63% of overweight, and 46.3% of obese women. The BMI categories in this analysis were based on the IOM definition of normal weight (19.8-26 kg/m²), overweight (26.1-29.0 kg/m²), and obese (> 29.0 kg/m²) [3]. It has been well documented in the literature that excessive maternal weight gain and poor maternal nutritional status show associations with negative birth outcomes in animals and humans [4-8].

Negative birth outcomes may include large for gestational age (LGA), excessive

adiposity, impaired cardiovascular development, increased waist to hip ratio, and adverse cardio-metabolic outcomes [4-6, 9, 10]. Nehring and colleagues (2013) suggested that approximately 5-13% of overweight and obesity prevalence in children can be attributed to excess maternal GWG [11]. The same study indicated that there was a 21% increased risk for overweight in children born to mothers who experienced excess GWG [11]. Overall, maternal obesity is associated with increased adverse outcomes for both mother and infant and an increased risk of long-term morbidity of children born to obese mothers [8].

Childhood obesity closely relates to prepregnancy overweight and obesity and excess GWG [4, 5, 11-13]. Maternal and childhood obesity rates have both been rising in past years [2]. For example, analysis of the NHANES 2009-2010 data showed an increased trend in overweight and obesity in males aged 2-19 from the NHANES 1999-2000 to the 2009-2010 data. Notably, this trend was not observed in females aged 2-19, indicating a difference based on sex [2]. Similarly, significant differences based on subgroup classification were observed. Specifically, the prevalence of overweight and obesity was highest among 12-19 year olds, with rates greater among non-Hispanic blacks, Hispanics, and males [2]. When observing obesity and overweight together for all groups, the prevalence was estimated to be 31.8% [2].

In infancy, an increase in fat mass is associated with GWG in excess of the IOM recommendations [14, 15]. Previous studies demonstrated strong associations with maternal GWG and childhood obesity and abdominal adiposity [13]. Overweight prevalence was shown to be two times higher and abdominal adiposity increased about 50% in children of mothers with excess GWG [13]. Additionally, results of a meta-

analysis by Gaillard et al. suggested a three-fold higher risk of obesity in children born to obese mothers [6].

Child birth weight is associated with childhood obesity, diabetes, and cardio-metabolic outcomes [16, 17]. Regarding child birth weight, classifications include small for gestational age (SGA) (<5.5pounds), appropriate for gestational age (AGA) (5.5-8.5 pounds), and large for gestational age (LGA) (>8.5 pounds) [18]. Curhan et al. reported an increased odds of a high BMI ($>29.2 \text{ m/kg}^2$) in women who had a high birth weight (8.6-10 pounds) [19]. This relationship was parabolic with both low and high birth weight groups at increased odds of the highest BMI category later in life ($>29.2 \text{ m/kg}^2$) [19]. A study by McCance et al. reported both low and high birth weights as strong predictors of the prevalence of diabetes later in life [20]. In an analysis of the Health Professionals Follow-up study, low birth weight (<5.5 pounds) was associated with an increased odds of developing diabetes and hypertension later in life, after adjusting for BMI [21]. Additionally, a high birth weight (≥ 10 pounds) resulted in a decreased odds of hypertension later in life, though not significant [21]. In the Nurses Health Study, low birth weight was associated with an increased odds of hypertension later in life, after controlling for BMI [19]. One proposed mechanism for this increase in hypertension is fetal vascular adaptations and remodeling related to intrauterine growth restriction (IUGR) [22]. Incidence of IUGR is higher in obese mothers, with characterization often as SGA [22, 23]. Overall, the association between birth weight and metabolic syndrome risk factors is well established in the literature [4, 16, 17, 19, 21, 22, 24].

Children who are obese with excess abdominal adiposity are more likely to have markers of metabolic dysfunction than normal weight children [4]. Metabolic dysfunction

represents a broader category than metabolic syndrome. According to the International Diabetes Federation (IDF), metabolic syndrome is defined as a waist circumference ($>90^{\text{th}}$ percentile) plus two of the following criteria: elevated triglycerides, low high-density lipoprotein cholesterol (HDL-C), elevated blood pressure, and elevated fasting glucose. Metabolic syndrome is used to classify individuals at an increased risk of cardiovascular disease and type 2 diabetes mellitus, yet does not include other important factors attributed to increased metabolic risk. Metabolic dysfunction is a more inclusive term and incorporates the following additional risk factors: elevated low-density lipoprotein cholesterol (LDL-C), elevated non-HDL cholesterol (non-HDL-C), insulin resistance, and elevated waist to height ratio (WHR) [25, 26]. The term metabolic dysfunction is used to classify children and adolescents at overall increased metabolic and cardiovascular risk [25, 26]. The associations between various markers of metabolic dysfunction, such as increased WHR, systolic blood pressure, and insulin resistance, have been linked to excessive GWG in various research studies and review articles [4-6, 13, 26]. Therefore, excessive GWG may have a negative impact for the child during development.

To date, there is still debate regarding the strength of the relationship between prepregnancy BMI and excess GWG. It appears that prepregnancy weight is more strongly associated with negative fetal outcomes, as compared to GWG [5]. However, the most predictive factors and the recommended lifestyle prevention strategies for addressing the associated metabolic consequences in children and adolescents are unclear [4, 5, 13].

The American Academy of Pediatrics (AAP) guidelines state for children and

adolescents to engage in 60 minutes of physical activity every day of the week [27-29]. Further studies documented the importance of various modes of physical activity, including structured sport, unstructured playtime, vigorous activity, and strengthening activities [28, 30]. Additionally, Peplies et al. reported an association between decreased physical activity levels, increased sedentary time, and the Homeostatic model assessment of insulin resistance (HOMA-IR), one of the markers of metabolic dysfunction [31]. Regarding sedentary time, the AAP recommends no more than 2 hours of screen time per day for children 5 and older [27, 29]. Limiting sedentary behaviors, most predominantly screen time, is essential for the prevention and reduction of obesity in this population [32, 33]. An increase in screen time and sedentary behavior is associated with increased waist to hip ratio, WHR, and waist circumference, known predictors of cardiovascular disease in children and adolescents [26, 32, 34]. Overall, these findings support the recommendations made by the AAP for lifestyle habits that support the health of a child.

Regarding dietary habits, the AAP guidelines include the promotion of daily breakfast consumption and the reduction of sugar-sweetened beverages [27]. Research that addresses daily breakfast consumption indicates a reduced risk of overweight and positive association with improved educational quality and learning outcomes during childhood [27, 35, 36]. Studies support breakfast consumption as an approach to decrease BMI in children and adolescents, an important factor when considering overall metabolic health [36-38]. Additionally, the AAP suggests that health promotion of lifestyle factors in the pediatric population be focused on the elimination of sugar-sweetened beverages from the diets of children [27, 29]. To date, there is a growing body of evidence to support the AAP recommendation on the elimination of sugar-sweetened beverages. For

example, de Ruyter et al. and Ebbeling et al. reported reductions in body weight in both normal weight and obese children when sugar-sweetened beverages were replaced with zero calorie beverages [39, 40]. Additionally, a meta-analysis by Vartanian et al. examined studies (n=88) assessing the association of soda consumption with nutrition and health outcomes. The authors concluded there was a clear association between sugar-sweetened beverage consumption and increased body weight, lower intake of essential nutrients, increased likelihood of developing diabetes, and increased systolic and diastolic blood pressure [41]. In summary, the literature suggests that behavior modification in these areas may impact the negative metabolic consequences contributed to by inappropriate prepregnancy BMI and excess gestational weight gain.

Significance of Problem

Childhood obesity, abdominal adiposity, and increased metabolic risk have been correlated with excess GWG in past research. However, to our knowledge, the associations between excess GWG and the parameters of metabolic dysfunction have not been researched exclusively under the aforementioned definition.

Purpose and Hypotheses of Research

The purpose of this study was to determine the relationship between maternal weight gain and metabolic dysfunction in obese children and adolescents in the STAGES study.

The specific aims for the research were:

1. Assess the associations between maternal weight gain, child birth weight, and

prepregnancy BMI with metabolic dysfunction in obese children and adolescents.

2. Determine the relationships among physical activity levels, dietary habits, and sedentary behavior with metabolic dysfunction in obese children and adolescents.

Regarding the first specific aim, we hypothesized that excess maternal weight gain during pregnancy would be associated with metabolic dysfunction in obese children and adolescents. We hypothesized that factors related to maternal weight gain, including child birth weight and prepregnancy BMI, would also be associated with the metabolic dysfunction observed in this obese population. The null hypothesis for this research was that there would not be an association between maternal weight gain, child birth weight, prepregnancy BMI, and metabolic dysfunction in this sample of obese children and adolescents. Regarding the second specific aim, we hypothesized that children and adolescents with a low level of physical activity, increased sugar-sweetened beverage consumption, limited breakfast consumption, and increased sedentary time would be more likely to have metabolic dysfunction. The null hypothesis for this research was that the aforementioned health behaviors would not be related to markers of metabolic dysfunction.

METHODS

Study Participants

Obese (BMI \geq 95th percentile for sex and age) children and adolescents aged 8-17 were recruited from pediatric clinics and community centers in Salt Lake City, Utah between July 15, 2010 and January 31, 2013. Data collection ended on March 31, 2015.

Inclusion criteria. Participants were all classified as obese according to the Centers for Disease Control and Prevention growth charts [42]. Additionally, participants were in good health other than insulin resistance, dyslipidemia, impaired glucose tolerance, or hypertension.

Exclusion criteria. Participants were excluded from the study for any of the following criteria: inability to speak English or Spanish; diagnosis of a genetic disorder or other syndrome known to cause obesity (Prader-Willi, leptin deficiency, hypothyroidism, Cushing Disease, Cystic Fibrosis); pregnant or history of pregnancy; cancer or history of cancer; active infectious disease; a history of cardiovascular disease or stroke during the previous 36 months; plasma triglycerides (> 400 mg/dL); diabetes mellitus (types 1 and 2); and the use of psychotropics, sulphonylureas, thiazolidinediones, atypical anti-psychotics, insulin, glucocorticoids, anti-neoplastic agents, angiotensin receptor blockers, or angiotensin converting enzyme inhibitors.

Study Design

This longitudinal study enrolled participants (n=124) who were evaluated once annually for up to 4 years. For the purpose of this analysis, baseline data were reported for participants with complete data. However, second visit data were used for participants with incomplete or missing breakfast and soda consumption data at baseline.

Anthropometrics. Weight was assessed with a digital scale in kg (Model 5002, Scale-Tronix, White Plains, NY) and height was measured with a stadiometer (Model Height-Rite 225, Seca, Culver City, CA) to the nearest 0.1 cm. Waist circumference was obtained by wrapping a tape measure snugly around the midsection at the umbilicus without compressing the skin. The measurement was recorded to the nearest 0.1 cm where the tape met. Height and waist circumference were each measured twice, and a third time if the two measurements deviated by greater than 1 cm. Waist to height ratio (WHR) was calculated from the waist circumference and height of the participant. BMI was calculated as kg/m^2 based on weight and height measurements. Blood pressure was assessed using an automated sphygmomanometer (Model Dynamap Pro 400, GE, Fairfield, CT), usually in the right arm. Measurements were taken twice. If the difference between measurements was greater than 5 mm/Hg, a third measurement was obtained and an average of all three was used. Trained research personnel performed all anthropometric measurements.

Biomarkers. After fasting for 12 hours, blood was obtained to measure serum levels of glucose, insulin, and a complete lipid profile. Serum insulin concentrations were measured in an enzyme-linked immunosorbent assay format (Alpco Diagnostics, Salem, NH; intra-assay precision: 1.0 – 7.4%, inter-assay precision 2.4 – 8.4%; sensitivity: 1.5

ng/mL; accuracy: 92 – 100%). Each assay was performed in duplicate, with a control for a standard. To analyze the sample, an ELISA assay was performed with a Luminex analyzer. Glucose was measured using a glucose analyzer. Insulin and glucose were used to calculate HOMA-IR, an estimation of insulin resistance with the following equation (fasting serum insulin ($\mu\text{U}/\text{m}$) x fasting plasma glucose (mmol l^{-1})/22.5) [43]. The analysis of serum lipid concentrations was conducted with a manual method (colorimetric for total cholesterol and triglycerides, dextran sulfate precipitation method for HDL-C). The Coefficient of Variation for total cholesterol and triglycerides were $< 2\%$, and for HDL-C, $< 5\%$. LDL-C was calculated using the Friedwald equation.

To fully understand the risk of CVD and metabolic consequences of excess GWG in our population, metabolic dysfunction was defined as the presence of one or more of the following: an increased WHR (≥ 0.5), LDL ≥ 110 mg/dL, non-HDL > 145 mg/dL, HOMA-IR ≥ 3.16 representing an increased insulin resistance, or any one of the markers of metabolic syndrome defined by the IDF: triglycerides ≥ 150 mg/dL, HDL < 40 mg/dL, blood pressure systolic ≥ 130 /diastolic ≥ 85 mm Hg, and fasting plasma glucose ≥ 100 mg/dL [26, 44]. During the analysis, metabolic dysfunction was redefined after finding that all but three participants had a WHR over 0.5. The inclusion of WHR made the definition not sensitive enough; therefore, for the purpose of analysis, this criterion was eliminated from the definition.

Lifestyle factors. An 80-item STAGES Participant Questionnaire was completed at each visit. Items were derived from the NHANES 2003-2004 edition and adapted for the current study [45]. Questions included demographic information, physical activity and nutrition habits, and health history. Physical activity was assessed using the Physical

Activity Questionnaire for older children (10-item) (PAQ-C) and adolescents (9-item) (PAQ-A) [46]. Questions included information regarding type, frequency, intensity, and time of exercise. This questionnaire was added two years into the study after discovering that it was more appropriate for the research than the questions from the STAGES questionnaire. Therefore, participants enrolled during 2012 took the PAQ at baseline while those enrolled previously did not. To standardize the scores from the PAQ, only questions that provided information on the number of days per week and hours per day that the participant was physically active were used. Then, those questions pertaining to the number of days per week were averaged to create a single score. Similarly, minutes per day were averaged to create one single score. The scores were then allocated to match the categories defined in the STAGES questionnaire. These categories are defined in the lifestyle factors section below. All questionnaire information was obtained by self-report from children and parents/guardians, depending on the age of the child.

Maternal prepregnancy BMI was classified as underweight ($< 18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$), class I obesity ($30\text{-}34.9 \text{ kg/m}^2$), and severe obesity ($\geq 35 \text{ kg/m}^2$) based on the World Health Organization definition [47]. Gestational weight gain was classified as: “Less than 25 pounds”, “25-30 pounds”, “More than 30 pounds”, “I don't know”, or “I prefer not to answer this question.” Classification of maternal weight gain was based on prepregnancy BMI and gestational weight gain (< 25 pounds, 25-30 pounds, > 30 pounds) to yield three categories: inadequate, appropriate, and excessive based on the IOM guidelines published in 2009 [3]. Birth weight was defined as low (< 5.5 pounds), normal ($5.5\text{-}8.75$ pounds), and high (> 8.75 pounds), according to the classifications of small for, appropriate for, and large

for gestational age [18].

Lifestyle habits were divided into multiple categories. Physical activity level was categorized into days per week and minutes per day. The days per week variable was defined as high (7 days per week), low (≤ 6 days per week), and none (0 days per week), with the minutes per day variable defined as high (> 30 minutes) and low (< 30 minutes) [27]. The AAP recommends 60 minutes of physical activity per day; however, few participants met this requirement. Thus, we defined high physical activity as 30 minutes for this particular sample [29]. Sedentary behavior consisted of hours of screen time, with categories defined as high (≥ 2 hours per day), low (< 2 hours per day), or none (0 hours per day). Dietary habits were based on the frequency of breakfast consumption per week (infrequent ≤ 6 days and frequent 7 days) and soda consumption per day was defined as never (0 drinks) and soda drinkers (≥ 1 per day).

Incentives. Participants obtained free lab results, as well as a \$20 gift card for each lab test visit.

Statistical Methods

The first aim of statistical analysis was to assess the associations between GWG, child birth weight, and prepregnancy BMI with childhood metabolic dysfunction. Children and adolescents were classified into two groups based on anthropometric and laboratory data, as presence or absence of metabolic dysfunction. The second aim was to determine the relationships between metabolic dysfunction and lifestyle habits in children and adolescents. Lifestyle habits were classified into the previously mentioned groups and compared with the presence or absence of metabolic dysfunction.

Descriptive characteristics obtained for the analysis included age, ethnicity, height, weight, and markers of metabolic dysfunction. The prevalence of metabolic dysfunction among the 124 participants was evaluated using a point estimate for one sample. The chi-squared and Mantel-Haenzel test statistic were used to examine the differences in proportions for the outcome of metabolic dysfunction based on GWG, child birth weight, prepregnancy BMI, physical activity, sedentary behaviors, soda consumption, and breakfast frequency individually. A 95% confidence interval ($\alpha=0.05$) was the level of significance.

Statistical analysis was performed using the SAS statistical software (version 9.4) (Cary, NC) [48]. Research electronic data capture (REDCap) (version 6.10.17) (Vanderbilt University) (Nashville, TN) was used for the electronic database and data record keeping [49].

RESULTS

Demographic and Participant Characteristics

Of the 124 enrolled participants, characteristics and demographic data were provided for 117 (51 male and 66 female) children and adolescents. Participants with incomplete records and duplicate records were excluded from the analysis. The average age of participants was 12.47 years. The mean BMI and BMI z-score were 29.29 kg/m² and 2.01, respectively. Over half of the participants (n=62) self-identified as Hispanic and the remaining (n=55) self-identified as non-Hispanic. The majority of mothers were normal weight (n=27) and overweight (n=14). Most of the remaining mothers were obese (n=9) or severely obese (n=9). Only two mothers were classified as underweight and 56 mothers preferred not to answer this question. Regarding maternal weight gain, the frequency was evenly distributed among the categories of inadequate (n=27), appropriate (n=27), and excessive (n=26). Additionally, 37 mothers either did not know how much weight was gained during pregnancy or preferred not to answer. A majority of participants in the study were normal birth weight (n=68), with the remaining categorized as high birth weight (n=21), low birth weight (n=7), and preferred not to answer (n=21). The maternal and child participant characteristics are displayed in Table 1.

Table 1. Participant characteristics of children (n=117) and mothers enrolled in the STAGES study

| Mothers | |
|--|-------------------------|
| Maternal Prepregnancy BMI | (%) |
| Underweight (<18.5 kg/m ²) | 3.28 (n=2) |
| Normal Weight (18.5-24.9 kg/m ²) | 44.26 (n=27) |
| Overweight (25-29.9 kg/m ²) | 22.95 (n=14) |
| Obese (30-34.9 kg/m ²) | 14.75 (n=9) |
| Severe obesity (≥ 35 kg/m ²) | 14.75 (n=9) |
| Missing | 56 |
| Maternal Weight Gain | (%) |
| Inadequate (<25 pounds) | 28.13 (n=27) |
| Appropriate (25-30 pounds) | 28.13 (n=27) |
| Excessive (>30 pounds) | 27.08 (n=26) |
| I don't know | 16.67 (n=16) |
| Missing | 21 |
| Children | |
| Age | Years |
| Mean ± SD ^a | 12.47 ± 2.5 |
| BMI^a | kg/m² |
| Mean ± SD | 29.29 ± 6.14 |
| Z-score | 2.01 ± 0.46 |
| Sex | (%) |
| Male | 43.59 (n=51) |
| Female | 56.41 (n=66) |
| Ethnicity | (%) |
| Hispanic | 52.99 (n=62) |
| Non-Hispanic | 47.01 (n=55) |
| Child Birth Weight | (%) |
| Low (<5.5 pounds) | 7 (n=7) |
| Normal (5.5-8.75 pounds) | 68 (n=68) |
| High (>8.75 pounds) | 21 (n=21) |
| Prefer not to answer | 4 (n=4) |
| Missing | 17 |

^aAbbreviations: BMI, body mass index; SD, standard deviation.

Lifestyle Factors

Of the 117 participants, complete data for physical activity days per week, minutes per day, and sedentary behavior was obtained for 88 participants. Regarding these participants (n=88), the majority were active less than 7 days per week (89.8%, n=79), with only 10.2% (n = 9) active 7 days per week. About half of the physically active children, 48.9% (n = 43), exercised more than 30 minutes per day. Nearly all of the children and adolescents, 93.2% (n=82), were highly sedentary, sitting for more than 2 hours per day. Regarding dietary habits, complete breakfast and soda consumption data were collected for a total of 59 and 57 participants, respectively. A greater proportion of participants ate breakfast every day, with 62.7% (n=37) of participants in the frequent group, as compared to 37.3% (n=22) in the infrequent group. Participants were almost evenly distributed in the soda consumption categories; 49.1% (n=28) drank soda at least once a day and 50.9% (n=29) never drank soda. The results for the physical activity level, breakfast pattern, and soda consumption data for enrolled children and adolescents are reported in Table 2.

Markers of Metabolic Dysfunction

Two participants were missing data for triglycerides, HDL, non-HDL, LDL, blood glucose, and HOMA-IR. Complete participant (n=117) data were available for the remaining biomarkers. Only one biomarker, HOMA-IR, had a mean value (4.73 ± 3.39) above the cutoff for a diagnosis of metabolic dysfunction. All other mean values were within a normal range. The means and standard deviations for the biomarkers were HDL (46.26 ± 10.27), non-HDL (118.23 ± 25.98), LDL (93.14 ± 19.84), triglycerides (124.53

Table 2. Physical activity and dietary habits for children (n=117) enrolled in the STAGES study

| Lifestyle Factors | (%) |
|----------------------------------|--------------|
| Physical Activity | |
| Days/week | |
| High (7 days) | 10.23 (n=9) |
| Low (≤ 6 days) | 86.36 (n=76) |
| None | 3.41 (n=3) |
| Missing | 29 |
| Minutes/day | |
| High (>30) | 48.86 (n=43) |
| Low (<30) | 51.14 (n=45) |
| Missing | 29 |
| Sedentary Behavior | (%) |
| High (>2 hours/day) | 93.18 (n=82) |
| Low (<2 hours/day) | 6.82 (n=6) |
| Missing | 29 |
| Frequency of Breakfast | (%) |
| Infrequent (≤ 6 days/week) | 37.29 (n=22) |
| Frequent (7 days/week) | 62.71 (n=37) |
| Missing | 58 |
| Soda Consumption | (%) |
| Never | 50.88 (n=29) |
| Soda Drinkers (≥ 1 /day) | 49.12 (n=28) |
| Missing | 60 |

± 65.57), systolic blood pressure (111.76 ± 11.56), diastolic blood pressure (66.2 ± 8.1), and blood glucose (91.76 ± 6.21). Based on the biomarkers, the prevalence of metabolic dysfunction in this group was 76.9% (n = 90). Mean values and standard deviations of the biomarkers for the diagnosis of metabolic dysfunction are reported in Table 3.

Weight Parameters and Presence of Metabolic Dysfunction

Children and adolescents born to women who were severely obese ($\geq 35 \text{ kg/m}^2$) before pregnancy had the highest prevalence (88.9%, n=8) of metabolic dysfunction among all BMI categories, although not statistically significant ($p=0.58$). There was no correlation between the prevalence of metabolic dysfunction in children and adolescents

Table 3. Mean values of biomarkers used to diagnose metabolic dysfunction (n=117)

| Metabolic Marker | Mean \pm SD |
|------------------------------------|--------------------|
| HDL (mg/dL) ^b | 46.26 \pm 10.27 |
| Non-HDL (mg/dL) ^b | 118.23 \pm 25.98 |
| LDL (mg/dL) ^b | 93.14 \pm 19.84 |
| Triglycerides (mg/dL) ^b | 124.53 \pm 65.57 |
| Systolic Blood Pressure (mmHg) | 111.76 \pm 11.56 |
| Diastolic Blood Pressure (mmHg) | 66.2 \pm 8.1 |
| HOMA IR ^b | 4.73 \pm 3.39 |
| Glucose* (mg/dL) ^b | 91.76 \pm 6.21 |
| WHR | 0.62 \pm 0.08 |

^a Abbreviations: HDL-C, high density lipoprotein cholesterol; HOMA-IR, homeostasis model of assessment-insulin resistance; LDL-C, low density lipoprotein cholesterol; SD, standard deviation; WHR, waist-height ratio.

^b Sample size for these variables is 115.

*Fasting Plasma Glucose

and GWG (p=0.81). There was a positive association between child birth weight and metabolic dysfunction (p=0.034). The prevalence of metabolic dysfunction was highest in the low birth weight group (85.7%, n=6), with lower rates in the normal birth weight group (80.9%, n=55) and high birth weight group (57.1%, n=12), respectively. Weight parameters and corresponding presence of metabolic dysfunction in children and adolescents are reported in Table 4.

Lifestyle Factors and Presence of Metabolic Dysfunction

Days of physical activity per week were not associated with the presence or absence of metabolic dysfunction (p=0.33). There was no difference in the diagnosis of metabolic dysfunction between children who were active for more than 30 minutes per day or less than 30 minutes per day (p=0.538). The proportion of participants with metabolic dysfunction was greater in the high sedentary (>2 hours per day) group (p=0.015), as compared with the low sedentary group (<2 hours per day). There was no

significant difference in the diagnosis of metabolic dysfunction between the frequent and infrequent breakfast groups ($p=0.69$). There was no significant difference between soda and non-soda drinker groups ($p=0.17$). The lifestyle factors and presence of metabolic dysfunction for enrolled children and adolescents are reported in Table 5.

Table 4. Weight parameters of children and mothers and corresponding presence of metabolic dysfunction

| Weight parameters | Percent of Participants with Metabolic Dysfunction (%) | P-value |
|--|--|---------|
| Overall Sample | 76.92 % (n=90) | 0.58 |
| Maternal Prepregnancy BMI | | |
| Underweight (<18.5 kg/m ²) | 50 % (n=1) | |
| Normal Weight (18.5-24.9 kg/m ²) | 77.78 % (n=21) | |
| Overweight (25-29.9 kg/m ²) | 78.57 % (n=11) | |
| Obese (30-34.9 kg/m ²) | 66.67 % (n=6) | 0.81 |
| Severe obesity (≥ 35 kg/m ²) | 88.89 % (n=8) | |
| Maternal Weight Gain | | |
| Inadequate (<25 pounds) | 81.48 % (n=22) | 0.034 |
| Appropriate (25-30 pounds) | 74.07 % (n=20) | |
| Excessive (>30 pounds) | 76.96 % (n=20) | |
| Child Birth Weight | | |
| Low (<5.5 pounds) | 85.71 % (n=6) | 0.034 |
| Normal (5.5-8.75 pounds) | 80.88 % (n=55) | |
| High (>8.75 pounds) | 57.14 % (n=12) | |

Table 5. Lifestyle factors of children and presence of metabolic dysfunction

| Lifestyle Factors | | P-value |
|-------------------------------|--------------|---------|
| Physical Activity | (%) | 0.33 |
| Days/week | | |
| High (7 days) | 88.89 (n=8) | |
| Low (≤ 6 days) | 72.37 (n=55) | |
| None | 100 (n=3) | 0.54 |
| Minutes/day | | |
| High (>30) | 77.78 (n=35) | |
| Low (<30) | 72.09 (n=31) | 0.015 |
| Sedentary Behavior | (%) | |
| High (>2 hours/day) | 78.05 (n=64) | |
| Low (<2 hours/day) | 33.33 (n=2) | 0.69 |
| Frequency of Breakfast | (%) | |
| Infrequent (≤ 6 days/week) | 68.18 (n=15) | |
| Frequent (7 days/week) | 72.97 (n=27) | 0.17 |
| Soda Consumption | (%) | |
| Never | 62.07 (n=18) | |
| Soda Drinkers (≥1/day) | 78.57 (n=22) | |

DISCUSSION

The prevalence of metabolic dysfunction in this group of obese children and adolescents was 76.9%. In a systematic review, Friend et al. reported a prevalence of metabolic syndrome of 29.2% in obese children, according to an analysis of 85 peer reviewed research articles [50]. Although metabolic syndrome is a less inclusive term, as compared to metabolic dysfunction, the prevalence in the Friend et al. study is significantly different from the sample in this study ($P < 0.0001$).

Another major study finding was the association between child birth weight and presence of metabolic dysfunction. Low birth weight was most strongly correlated with a diagnosis of metabolic dysfunction, as compared to all other birth weight categories. This result is consistent with past research demonstrating an inverse correlation between low birth weight and increased vascular dysfunction, insulin resistance, and obesity, which are markers of metabolic dysfunction [4, 22, 51]. Specifically, Curhan et al. reported that men with a birth weight of <5.5 pounds had a 1.88 greater odds of diabetes, as compared to men with a birth weight of 7.0-8.4 pounds [21]. Additionally, in a Nurses Health Study analysis, Curhan et al. reported an increased odds (OR, 1.42) of hypertension in women who were <5.5 pounds at birth, as compared to the reference category (7.1-8.5 pounds) [19]. In the present study, high birth weight, as compared to low and normal birth weight, was least associated with metabolic dysfunction. This finding is contradictory to past studies that demonstrated a U shaped relationship between birth weight and metabolic

dysfunction. A review by Gaillard et al. reported an association between high birth weight and obesity later in life [4]. In the same paper, the authors reference an association between both low and high birth weight and increased risk of obesity, type 2 diabetes, and cardiovascular dysfunction [4]. Also, McCance and colleagues demonstrated a parabolic association ($p < 0.05$) between diabetes and birth weight, studied as a continuous variable, using logistic regression analysis [20].

Contrary to the study hypothesis, a higher prepregnancy BMI was not significantly associated with the presence of metabolic dysfunction. However, children born to mothers who were obese at the time of conception had a higher prevalence of metabolic dysfunction, though not significant. Increased prevalence of metabolic dysfunction in children born to mothers with prepregnancy obesity has been found in the literature. Gaillard and colleagues reported the results of a meta-analysis showing a three-fold increased risk of obesity in children born to mothers with prepregnancy obesity [4]. Additionally, Hull et al. demonstrated that maternal prepregnancy obesity was a strong predictor ($p = 0.001$) of increased infant fat mass [14].

There was no association between excess GWG and metabolic dysfunction in the current study. Children and adolescents born to mothers who gained appropriate weight during pregnancy had a lower prevalence of metabolic dysfunction, as compared to the other groups, though not statistically significant. This finding is contrary to past research that did detect a significant association between GWG and markers of metabolic dysfunction [4-6, 11-15]. Gaillard et al. reported that higher GWG in early pregnancy was associated with increased childhood BMI, total fat mass, and systolic blood pressure ($p < 0.05$ for all variables) [5]. Results from the same study demonstrated that GWG in

early pregnancy was independently and positively associated with cardio-metabolic risk factors in children ($p < 0.05$) [5]. Furthermore, a meta-analysis by Nehring et al. showed an increased odds (OR, 1.38) of childhood overweight and obesity when mothers gained excess gestational weight [11].

Regarding lifestyle factors, only sedentary behavior was associated with the presence of metabolic dysfunction. Absence of significant findings between physical activity, breakfast frequency, soda consumption, and the outcome variable were contrary to the study hypothesis. Participants who were physically active every day, and for more than 30 minutes a day, did not have a lower prevalence of metabolic dysfunction than the other groups. This result conflicts with past studies that demonstrate the health benefits of physical activity in children and adolescents [28, 31]. Pepiles et al. reported lower odds of developing insulin resistance in children engaging in ≥ 54.6 minutes of moderate to vigorous physical activity per day, as compared to the reference group (< 27 minutes/day) (OR, 0.7) [31]. The U.S. Department of Health and Human Services recommends physical activity to reduce the risk of hypertension, diabetes, and cardiovascular disease [28]. These proposed benefits would result in a lower risk of metabolic dysfunction, which was not observed with increased physical activity in the present study.

The positive correlation between low sedentary behavior and a decrease in metabolic dysfunction has been supported in previous research. Robinson and colleagues reported a significant reduction in BMI ($p = 0.002$) and waist circumference ($p < 0.001$), as compared to controls, after an intervention aimed at reducing television viewing [32]. Significant differences between the high and low sedentary groups, yet not physical activity groups, supports previous findings that the message of reducing sedentary time

produces greater behavior change than increasing physical activity in children [33]. Warren and colleagues reported a 64% greater risk of dying from CVD in men who reported sitting for more than 23 hours per week [52]. Additionally, Epstein et al. reported a significant decrease in percent overweight ($p < 0.05$) and percent change in body fat ($p < 0.05$) in a group that reduced sedentary behavior, as compared to a group that increased physical activity over a 12-month period [33]. In this population of obese children, those who were less sedentary had a significantly lower prevalence of metabolic dysfunction. Also, the incorporation of physical activity did not have a significant effect on metabolic health in this population.

Children who never drank soda had a slightly lower frequency of metabolic dysfunction than those who did; however, this result was not significant for the current study. Those children who ate breakfast every day had a higher prevalence of metabolic dysfunction, as compared to children who did not, although not significant. This result was unexpected in that it contradicts previous research on the benefits of consistent breakfast consumption and limiting soda intake to reduce criteria of metabolic dysfunction [36-41]. The missing data for lifestyle factors may have contributed to the unexpected results or lack of significance in the current study.

A major strength of this research is the study population. All of the children enrolled in the study were obese. Additionally, a large proportion of participants were Hispanic. One study weakness was the introduction of the Physical Activity Questionnaire in year 2. At study initiation, the STAGES participant questionnaire, designed specifically for this study, was used. However, the PAQ better suited the research question than the STAGES participant questionnaire due to more detailed items

on physical activity habits. Also, lifestyle factors, maternal weight, and birth weight were obtained via self-report, with associated missing data and potential for inaccuracies. Furthermore, the study employed a convenience sampling method; thus, the enrolled participants did not represent a random sample of children living in the United States.

This research may be used to guide intervention efforts aimed at reducing childhood obesity. Specifically, interventions aimed at the maintenance of a healthy weight prior to and throughout pregnancy may help reduce the incidence of excess GWG. This research also seeks to provide evidence for the importance of implementing healthy lifestyle habits during childhood and adolescence. The focus on lifestyle factors that promote a healthy weight is important in the context of childhood obesity and metabolic dysfunction.

CONCLUSION

To date, the literature suggests that there is an association between sedentary behaviors and metabolic health, even in absence of weight loss. This study supports the rationale for interventions to reduce sedentary behaviors in obese children and adolescents. This research also indicates that low child birth weight is inversely correlated with a diagnosis of metabolic dysfunction, a finding not observed with prepregnancy BMI and GWG. Future research on the interaction between prepregnancy BMI, GWG, and child birth weight in the context of metabolic dysfunction is recommended.

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